Roche

Pharmaceuticals

00D-1539
Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1060
Rockville, MD 20852

U.S.A

Basel, December 3, 2002
Comments regarding Your Draft Guidance: "Electronic Records; Electronic Signatures, Maintenance of Electronic Records" (Docket No. 00D-1539)

Dear Madam, Dear Sir,

Thanks for the opportunity to comment on this guidance.

Your guidance was internally forwarded to a Roche expert group for electronic records and signatures for comments. This expert group has roughly 50 members from various countries. Please find enclosed the consolidated comments from this group.

We would suggest that this important guidance is also used to clarify under what circumstances the typewriter rule could be applied. We believe that this would be very helpful, because we are having lots of different understanding about the respective comment 22 of the preamble of 21 CFR Part 11 and when having a look at the various discussion forums we find that nobody is really sure how to interpret it.

The case is clear if an electronic record is never printed out and signed electronically. The electronic record represents then the master data in these cases. If an electronic record is printed we should distinguish between a hardcopy that was made for the only reason to sign or a hardcopy that was made to use as a form sheet to fill in the information. The printing process could be named as transformation, because it transforms electronic information to a paper record.

Auxiliary transformation is used for systems not yet capable to wear electronic signatures. An examples would be an Electronic Batch Recording (EBR) System, where the final signatures are performed as handwritten signatures on electronic records. The data resides on the system and is used from their to do further processing. Though the electronic records represent the master data.

One way transformation is used to print templates or forms that are necessary for documentation that needs to be recorded immediately. Such forms with handwritten entries are afterwards the records that should be archived and kept as part of the GMP-documentation.

00D-1539 C13

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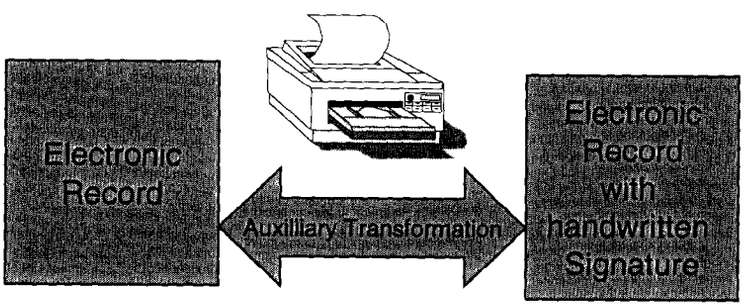
The paper is the master record.

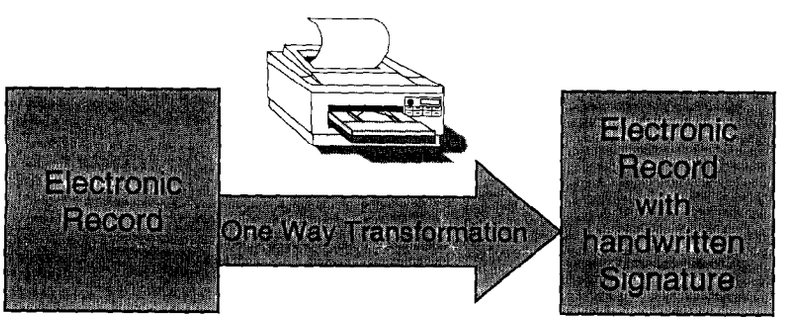
Example: EBR



Master

Archive Both
Auxiliary
Transformation
only to apply
Signature

Example: Forms, Templates



Master

Archive only
Protocol
Typewriter
Rule
applies

In essence the master should guide the archiving and maintenance practice. If the master is the filled in form, the filled in form needs to be kept. If the master is the electronic record, because it is afterwards used for further processing then the auxiliary transformation to the paper helps only as a tool to apply the signature.

1. *Chapter 2.1 Applicability (p3)*
Current draft: " Most predicate rules are contained in Title 21 of the Code of Federal Regulations."
Suggested text: " Predicate rules are contained in Title 21 of the Code of Federal Regulations."
Reason: All predicate rules applicable for GxP are in Title 21. Other rules e.g. finance reporting should not become relevant for 21CFR11.
Comment: The scope becomes clearer. If other rules should also be relevant, it would be of help for the industry to know which ones are meant explicitly.

2. *Chapter 4.1 What Does Part 11 Require? (p4)*
Current draft: "Here are some examples:"
Suggested text: "Here are the most important requirements"
Reason: The limitation to the most important requirements shows that if other requirements are not fulfilled a procedural solution would be acceptable.
Comment: Some commercial widely used systems have sometimes difficulties to reach compliance.

3. Chapter 4.1 What Does Part 11 Require? (p6)
Current draft: Reference to 11.50 and 11.70
Suggested text: Leave away these references
Reason: Electronic Record Maintenance is only optionally related to signatures
Comment: In the case of handwritten signatures to electronic records a the record is transformed from electronic to paper based. In this case there are two possibilities. Either the paper record becomes the master or the electronic record becomes the master. If the paper record is the master, the paper record should be mandated to be kept. If we have a validation protocol, the entry of handwritten records changes the validation protocol to a handwritten record. If on the other hand a record is signed by hand but the master data resides in a system, e.g. a lab worksheet is signed of but the data is not taken from the worksheet but from the memory of the system then the electronic record and the handwritten record need to be kept.

4. Chapter 5.3 Continued Availability And Readability Of Electronic Record Information Should Be Ensured.(p 8)
Current draft: You should periodically access a representative number of electronic records to ensure that record contents can still be read and evaluated throughout the records retention period.
Suggested text: You should follow the instructions of the storage device vendor to ensure that record contents can still be read and evaluated throughout the records retention period.
Reason: It is scientifically not possible to rely on a period or a number of records to check if they are still readable.
Comment: It does not make scientific statistical sense to take a small sample, because information must be 100% present or there is the risk that everything becomes unusable. Such testing is not representative by no means. The scientific evaluation of durability should be at the vendors who specifies the storage device. In addition handling of storage devices like CD-ROM bears the risk that these are damaged during handling, e.g. fall on the floor and crack. Frequent handling of magnetic tapes bears also the risk of aging, loss and mechanical destruction.

5. Chapter 5.5 The Ability To Process An Electronic Record's Information Throughout Its Records Retention Period Should Be Preserved. (p 10)
Current draft: The Ability To Process An Electronic Record's Information Throughout Its Records Retention Period Should Be Preserved
Suggested text: An Electronic Record should be readable throughout Its Records Retention Period
Reason: The preservation of functionality is sometimes illusion. Hardware may break down and succeeding systems with much better functionality may have taken over the task of the old equipment.
Comment: In exceptional cases the data needs to be defined for GMP-Critical data. E.g. it should be possible to generate a recall list.

6. Chapter 6.1 The Time Capsule Approach (p 12)
Comment: Unfortunately some software suppliers say that there is no more support for a system after a certain day. It would be fine to see in this guidance that such outdated systems still can be used even though the supplier denies any support.

7. Chapter 6.2.1.5 Unavoidable Differences And Losses Should Be Accounted For and Explained In The Migrated Electronic Record Or New System Documentation.(p 20)
Current draft: Just prior to performing the electronic record migration a trusted third party from outside of the organization that has some responsibility for the electronic record verifies the digital signature using the old system methods;
Suggested text: Just prior to performing the electronic record migration the digital signatures

are verified using the old system methods;
Reason: As the pharmaceutical company has the ultimate responsibility such a migration could also be done in house.
Comment: There will be tools available that are doing such migrations better that a "Trusted Third Party". It is not defined what such a third party is.

8. Chapter 6.2.1.3 Electronic Record Integrity Attributes Should be preserved (p18)
Current draft: 1. "Where a migration, in effect, creates a new electronic record (by transforming the old electronic record) then, per section 11.10(e), the audit trail for the migrated electronic record would have to cover this creation".
Suggested text: add: "The audit trail still needs only to record operator actions and not machine entries (11.10.e)
Reason: If this is the case whenever we migrate the Database version we could understand we are creating new electronic record. Lets think about a LIMS or ERP, we could therefore believe that with an database version upgrade we are creating new master batch records, bills of material, items, etc. And therefore we should include in the audit trail of each batch, item of a bill of material , etc.. an entry tracing that the record was updated due to an database version upgrade.
Comment: This paragraph has to be carefully revised, because a version upgrade is not necessarily changing the content of the already created record, and therefore we are not creating a new record. One should distinguish a system migration (for instance move from one ERP to another ERP) from a normal system upgrade. Maintaining records has more than the two poles black (The time capsule approach, which is impossible) and white (the record migration approach). This is to enable some "gray area" but keeping the intention to comply with the predicate rule.

9. Chapter 6.2.1.5 Unavoidable Differences And Losses Should Be Accounted For and Explained In The Migrated Electronic Record Or New System Documentation.(P 20)
Current draft: "trusted third party"
Suggested text: Remove this term
Reason: The term "has some responsibility" is unclear
Comment: Trusted third parties are not defined.

10. Chapter 6.3. Keeping printed hardcopies in exceptional cases.
Current draft: (does not exist)
Suggested text: If there are no further measures to keep a system alive it should also be possible to print out the data of an old retired system and to archive the paper during retention time. Alternatively these records could also be printed as *.PDF files.
Reason: Sometimes there is technically no other solution that makes any sense
Comment: There should always exist this final option, if the responsible departments including QA agree that this is the way to go. Example: After the earthquake in Kobe 1995 (Japan) all the data in a pharmaceutical plant was destroyed. Only the paper remained. Under this circumstances management has decided that the electronic data was not restored.

Yours sincerely,

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